

Remarks

Status of the Claims

Claims 2, 3, 8, 9, 22, 39, 42-47, and 49-58 are pending and under examination.

Claims 8, 9, 39, 44-46, and 51-59 are rejected.

Claims 2, 3, 5, 39, 42, 46, 47, 49, 55, and 58 are objected to.

Claims 2, 3, 42, 47, 49, 50, and 51 are amended to recite in line 3 “wherein the chimeric promoter comprises.”

Claim 2 is amended for consistency; all “*cis*” language is italicized.

Claims 3 and 49 are amended to recite “(iii) a *cis*-acting element having the nucleotide sequence.”

Claim 39 is amended to recite “A chimeric promoter to render a gene responsive to pathogens, obtained by a method comprising.”

Claim 39 subsets (1) and (2) are amended to recite “the at least one *cis*-acting element mediates induction of local gene expression in plants upon the pathogen elicitor treatment, the pathogen infection, or both to between.”

Claim 42(i) is amended to recite in line 6 “wherein the two or more *cis*-acting elements.”

Claims 46, 55, and 58 are amended to recite “the chimeric promoter” and to replace “and/or” in the last sentence with “or.”

Claim 52(i) is amended to include the language “wherein the second *cis*-acting element is a *cis*-acting element different from a CAAT element.”

Applicants thank the Examiner for expediting examination by examining the improperly submitted amendment of January 5, 2010.

Claim Objections

The Examiner objects to claims 2, 3, 39, 42, 46, 47, 49, 50-52, 55, and 58 for matters of consistency. Applicants amend the following claims in accordance with the Examiner's recommendations:

- The Examiner notes that each of claims 2, 3, 42, 47, 49, 50, and 51 should be amended to recite in line 3 "wherein the chimeric promoter comprises." Claims 2, 3, 42, 47, 49, 50, and 51 are accordingly amended.
- The Examiner notes that claims 3 and 49 refer to a chimeric promoter comprising (i) two or more *cis*-elements and (ii) a minimal promoter. The claims also recite "further comprising" which is in reference to the chimeric promoter. Applicants amend claims 3, 49, and 51 to recite "(ii) a *cis*-acting element having the nucleotide sequence" and delete the "further comprising" language.
- The Examiner notes that the preamble of claim 39 "should indicate that the promoter is a chimeric promoter. As well, the promoter is not obtained by a method of rendering a gene responsive to pathogens but is designed to form such a function." Applicants accordingly amend claim 39 to recite "A chimeric promoter to render a gene responsive to pathogens, obtained by a method comprising."
- The Examiner notes that claim 39 subsets (1) and (2) should be amended for consistency. Applicants accordingly amend claim 39 subsets (1) and (2) to recite "the at least one *cis*-acting element mediates induction of local gene expression in plants upon the pathogen elicitor treatment, the pathogen infection, or both to between."
- The Examiner notes that claim 42(i) should be amended to recite in line 6, "wherein the two or more *cis*-acting elements." Claim 42(i) is accordingly amended.
- The Examiner notes that claims 46, 55, and 58 recite "introducing a chimeric promoter" into the plants whereas when referring to previously recited limitations it is proper to use the article "the" as opposed to "a". Applicants accordingly amend claims 46, 55, and 58 to recite "--the chimeric promoter--."

- The Examiner also notes that the use of “and/or” in the last sentence of claims 46, 55, and 58 is inconsistent with the recitation of only “or” in the preamble. Applicants accordingly amend claims 46, 55, and 58 to remove “and/or” and replace it with “or.”

Claim Rejections – 35 USC § 112, first paragraph

The Examiner rejects claims 8, 9, 39, 44-46, 51 and 53-59 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner notes that this is a new rejection necessitated by Applicants’ amendments. Specifically, the Examiner asserts that the specification does not support the combinations of SEQ ID NO:11 with SEQ ID NOs:5, 6, 8, 9, 10, 12, and 13.

Applicants respectfully traverse.

In order to fulfill the written description requirement for every combination of the fourteen SEQ ID NOs as dimers, 196 combinations would need to be listed. This is also true for tetramers and octamers. Not counting possible hexameric combinations of a dimer, a list of 588 combinations would be required.

A person having ordinary skill in the art (“PHOSITA”) would understand from the sentence “homo and/or hetero-multimeric forms of SEQ ID NO:3-16” that these combinations are possible and within the scope of the present invention. A PHOSITA would further understand from the examples (not only Example 5) that these elements function as pathogen-responsive switches when used singly or as homo-multimeric forms. A PHOSITA would further understand from Example 5 that these elements can be mixed with each other and still function as pathogen-responsive switches. Indeed, a PHOSITA would have no doubt that combinations not actually covered by Example 5 would also function as pathogen responsive switches. In order to demonstrate the underlying principle that these elements function, in combination, as pathogen-responsive switches, fourteen (14) combinations were tested experimentally. To a PHOSITA, this represents proof of the concept that there exists a “toolbox” of responsive elements from which to build functioning chimeric promoters.

Applicants respectfully assert that the specification leaves no doubt that protection is sought for any combination of the disclosed *cis*-elements. Further proof of this is shown by the

claims as originally filed. Support for every conceivable combination of *cis*-acting elements comes from the following claims and paragraphs of the specification:

(A) Claims 1 – 3 of the application as originally filed:

1. A chimeric promoter capable of mediating local gene expression in plants upon pathogen infection comprising
 - (i) at least one *cis*-acting element sufficient to direct elicitor-specific expression comprising the nucleotide sequence of any one of SEQ ID NOS: 3 to 16, and
 - (ii) a minimal promoter.
2. The chimeric promoter of claim 1, further comprising a *cis*-acting element having the nucleotide sequence of SEQ ID NO: 1 or 2.
3. The chimeric promoter of claim 1 or 2, wherein said synthetic plant promoter comprises homo- and/or hetero-multimeric forms of said *cis*-acting element(s).

Claim 1 of the application as originally filed (PCT/EP99/08710) is related to chimeric promoters comprising at least one *cis*-acting element of any SEQ ID NOs: 3 to 16; in conjunction with claim 3, further specifying that the promoter may comprise homo- and/or hetero-multimeric forms of these *cis*-acting elements.

(B) Page 4, 5th paragraph:

“Eleven *cis*-acting elicitor-responsive elements (SEQ ID NOS: 3 to 13) were identified in accordance with the present invention. Monomers and multimers of each element were constructed in addition to synthetic promoters consisting of two or more of these elements [SEQ ID NOS: 3-13] in combination.”

(C) Page 5, 3rd paragraph:

“The experiments performed in accordance with the present invention demonstrate that the *cis*-acting elements [of the invention, SEQ ID NOs: 3-16] direct pathogen-induced expression *in vivo*, being active as monomers, multimers and in combination

with each other within synthetic promoters.”

(D) Page 6, 4th paragraph:

“ . . . the chimeric promoter comprises homo- and/or hetero-multimeric forms of said *cis*-acting element(s)”

(E) Page 7, 3rd paragraph:

“Thus, the present invention for the first time provides a generally applicable method for how to construct and use chimeric promoters in the field of plant biotechnology.”

(F) Page 22, 3rd paragraph:

“The present invention for the first time demonstrates that a number of *cis*-acting elements that are responsible for inducibility of pathogenesis-related genes can be used either alone or in combination with themselves or with other *cis*-acting elements to construct chimeric promoters that are capable of mediating highly inducible gene expression in plant cells upon elicitor treatment. It is therefore evident that *cis*-acting elements derived, e.g., from pathogen-related promoters other than those specifically described above can be used in accordance with the present invention, for example, chitinase promoters; see, e.g., Kellmann, Plant. Mol. Biol. 30 (1996), 351-358. Appropriate promoters that provide a source for such *cis*-acting elements can be used and obtained from any plant species, for example, maize, potato, sorghum, millet, coix, barley, wheat and rice. Such promoters are characterized by their inducibility upon pathogen infection.”

Hence, excluding specific combinations that are not reflected verbatim in the specification disregards what a PHOSITA would identify to be within the scope of the present invention.

Applicants also respectfully point to the following relevant sections of the MPEP:

(A) MPEP § 2163 I.B:

“While there is no *in haec verba* requirement, newly added claim limitations must be

supported in the specification through express, implicit, or inherent disclosure”
(emphasis added).

(B) MPEP § 2163 II.A.2:

“Prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, the examiner should review the claims and the entire specification, including the specific embodiments, figures, and sequence listings, to understand how applicant provides support for the various features of the claimed invention” (emphasis added).

(C) MPEP § 2163 II.A.3(a):

“Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.”

Also, “*In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (“To establish inherency, the extrinsic evidence ‘must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.’”

Applicants believe that the application as a whole lets a PHOSTIA understand that the *cis*-acting elements disclosed in the application and used in Examples 1 – 4 and 6 can be used in

any combination in order to form chimeric promoters, including those specific combinations listed in amended / new claims introduced in our last response filed January 5, 2010.

Page 40, 5th paragraph, of the specification as filed (*see also* Figure 8), emphasizes that the chimeric promoters are inducible by all potential pathogens, “and not just those for which there is already a functional defense system in operation in the plant.” It is further added on page 41 that “the *cis*-acting elements of the present invention show inducible expression in a heterologous plant” and that “this clearly shows that these elements could be functional in all plants.”

With respect to enablement, it is preemptively held that the specification provides, on page 36 (as filed), that the elements nearest to the TATA box (*i.e.* those mentioned last in the combinations) have the greatest effect on both level of expression and fold induction. From the foregoing Examples 1 and 2, one can see that 4 times element D (SEQ ID NO:11) is a strong “expresser” with a lower induction, whereas 4 times element S (SEQ ID NO:7) is a low “expresser,” but is highly inducible. Knowing that the latter element in the combination has the strongest effect on the combination, one clearly would expect that 4xD/4xS has a higher inducibility than 4xS/4xD. This is exactly the result obtained by and shown in Example 5, table on page 37, lines 8 and 10.

The same logic applies for the combination of 4 times element D (SEQ ID NO:11) with 4 times element W2 (SEQ ID NO:4). Also in this case, the element with the higher inducibility is placed near the TATA box (*i.e.* the combination 4xD/4xW2) – as this combination has a higher induction level – whereas a combination with the inverse orientation of elements (4xW2/4xD) has the higher expression level without elicitor, as would be expected from the values given for the tetramers of the elements given in Examples 2 (element D, SEQ ID NO:11) and 4.2 (element W2, SEQ ID NO:4). The fact that neither combination exceeds a 15-fold induction can be accounted to the extremely high level of expression without elicitor.

Additionally, the specification continues guiding the PHOSITA on page 36, last paragraph, recommending the use of spacers in order to avoid or reduce the observed and documented effects of steric hindrance.

Moreover, the specification clearly states on page 37 (under the table of Example 5) that “adding more copies of an element in a composite construct often increases the absolute level of expression, but often lowers the fold induction.”

All of the above recommendations given in the specification to the PHOSITA arise from the experimental data provided in the various examples.

Finally, it should be noted that out of the 14 combinations of Example 5, all combinations yield an inducible chimeric promoter, 13 exhibit an induction level of more than 10 fold (this is 92% of the tested combinations), and that 10 combinations out of the 14 exhibit an induction level of 18 fold or more (this is 71% of the tested combinations). If one takes into account the other examples of non-composite combinations (*i.e.* homo-dimers and tetramers) exclusively presented in the specification, the above rates would be even more favorable.

Thus, from the teachings of application as a whole, a PHOSITA would have no undue burden to produce promoters comprising further *cis*-element combinations with an expected rate of success that is rare in the biological field. A specific test for not literally described combinations of elements can be found on page 28 of the specification.

To the extent that the Examiner is inclined to object that the specification of SEQ ID NO:11 as a “mandatory element” is not so disclosed in the specification, it is reminded that the “selection” of SEQ ID NO:11 was due to a restriction requirement, not by Applicants’ independent election.

Hence, Applicants assert that the specification as a whole fulfills the written description requirement and respectfully request removal of §112 written description rejections. Additionally, it is also respectfully asserted that no additional §112 enablement rejections should issue.

Claim Rejections – 35 USC § 102(b)

The Examiner rejects claims 9, 39, 44-46, 52 and “56-59” under 35 U.S.C. § 102(b) as being anticipated by van de Locht et al (EMBO J, 1990, vol 9(9) p 2945-2950; see entire document). This is a new rejection necessitated by applicants' amendment by addition of “new claim 51” and to amendment to claim 39 wherein both recite a chimeric promoter comprising SEQ ID NO:1 (part 5 of claim 39).

The Examiner asserts that “van de Locht et al teach a promoter obtainable by insertion of pPR2-10, which comprises at least one *cis*-acting element sufficient to direct elicitor-specific expression into the promoter of the GUS reporter gene as recited in claim 39. pPR2-10 comprises SEQ ID NO:1 as indicated in figure 5 which demonstrates that pPR2-10 comprises the region from -168 to -43. This region comprises SEQ ID NO: 11 and functions as a *cis*-element sufficient to direct elicitor specific expression with the CAAT element. Hence the vector comprises at least two-*cis* acting elements wherein the sequences of SEQ ID Nall and CAAT are separated by at least 50 bases.”

Applicants first note that there is no claim 59; therefore, Applicants assume the Examiner means claims 9, 39, 44-46, 52, and 56-58 and respond accordingly. Next, Applicants note that the Examiner does not specifically reject claim 51 (“claims 9, 39, 44-46, 52, and 56-58”), but refers to claim 51 by saying “This is a new rejection necessitated by applicants’ amendment by addition of new claim 51” Applicants assume that the Examiner means to reject claim 52 under this section, and not claim 51, and respond accordingly.

In response to the § 102(b) rejection, Applicants point out that van de Locht et al. do not teach all claims limitations of claims 39(5) and 52 (as amended).

The objections of the Examiner are based on two constructs of van de Locht:

(A) pPR2-10 (Fig. 5):

This is a shortened version of the PR2 gene that contains, in addition to SEQ ID NO:11, another “*cis*-acting element” (the CCAAT Box, positions -91 to -86) in front of the natural promoter.

(B) pPR2-CHS (Fig. 6):

This is a chimeric promoter containing the CCAAT Box, SEQ ID NO:11, and a CHS minimal promoter, driving a GUS reporter gene.

Applicants point out that the CAAT Box is an element that is found in a vast variety of eukaryotic promoters and is located approximately 75 base pairs upstream from eukaryotic transcription start sites. This sequence is one of those that enhance binding of RNA polymerase (*see* search for CAAT at <http://bioinformatics.psb.ugent.be/webtools/plantcare/html/>). It is

questionable to refer to this sequence as a *cis*-acting element at all. However, Applicants overcome the rejection over van de Locht et al. in the following discussion.

As to (A), Applicants note that the promoter pPR2-10 referred to is not a chimeric promoter (claim 39(5)), nor is it a minimal promoter as required by claim 52. The promoter of pPR2-10 is a shortened version of the natural promoter of the PR-2 gene. Hence, pPR2-10 was not obtained by insertion of a *cis*-acting element (as required by claim 39). The promoters of Figure 5 of van de Locht et al. are all shortened versions of the natural promoter. The natural PR-2 promoter is not a minimal promoter.

As to (B), the only chimeric promoter described by van de Locht et al. is depicted in Figure 6 (pPR2-CHS), and it does not contain a minimal promoter. However, this pPR2-CHS construct also does not anticipate claim 39 as amended, as the chimeric promoter of pPR2-CHS does not drive a CHS gene. Claim 39 relates to promoters that drive their natural genes, which promoters are modified by insertion of *cis*-elements to make the expression of the natural gene of the promoter pathogen sensitive. In the construct of van de Locht et al., the HCS promoter drives a heterologous GUS gene, which is not the natural gene behind the CHS promoter. Hence, the construct described by van de Locht et al. in Figure 6 differs from those constructs described in claim 39 (as amended).

Claim 52 as amended specifies that the further *cis*-acting element is not a CAAT box. Hence, the amended claim also escapes the disclosure of van de Locht et al.

Finally, Applicants direct the Examiner's attention to the 37 C.F.R. § 1.132 Declaration filed by Applicants on March 12, 2007, in which one of the inventors, Imre Somssich, explains the distinctions between the van de Locht reference and the presently claimed invention.

Claim Rejections – 35 USC § 103

The Examiner rejects claims 9, 39, 44-46, 52 and "56-59" under 35 U.S.C. § 103(a) as being unpatentable over van de Locht et al (EMBO J, 1990, vol 9(9) p 2945-2950; see entire document) in view of Pears and Williams (Nucleic Acids Research, 1988, Vol 16(17), pages 8467-84861; see entire document) and Searle et al, MCB, 1985, Vol 5(6), pages 1480-1489; see entire document) further in view of Comai et al (Plant Molecular Biology, 1990, Vol 15(3), pages 373-381; see entire document). This is a new rejection necessitated by applicants'

amendment by addition of “new claim 51” and to amendment to claim 39 wherein both recite a chimeric promoter comprising SEQ ID NO:1 (part 5 of claim 39). The Examiner asserts that

it would have been obvious to one of ordinary skill in the art at the time the invention was made to duplicate the isolated promoter fragment that is elicitor responsive as taught by van de Locht et al as taught by Pears and Williams and Searle et al and Comai et al because and van de Locht et al teach that a fragment of the PR2 promoter is responsible for strong elicitor mediated gene activation and because Pears and Williams and Searle et al teach that multiple elements are more effective than single elements and Comai et al teach that it is within the ordinary skill of the art to generate chimeric vectors in which larger promoter elements are duplicated.

Applicants first note that there is no claim 59; therefore, Applicants assume the Examiner means claims 9, 39, 44-46, 52, and 56-58 and respond accordingly. Next, Applicants note that the Examiner does not specifically reject claim 51 (“claims 9, 39, 44-46, 52, and 56-58”), but refers to claim 51 by saying “This is a new rejection necessitated by applicants’ amendment by addition of new claim 51” Applicants assume that the Examiner means to reject claim 52 under this section, and not claim 51, and respond accordingly.

In response, Applicants again emphasize that van de Locht et al. have not discovered the importance of SEQ ID NO:11 as a elicitor sensitive *cis*-acting element. This is evident, for example, in page 2947, left column, last paragraph:

These data show, that the 116 bp between positions -168 and -52 of the PR2 promoter are necessary for elicitor-mediated expression of the gene.

These 116 bp do not contain SEQ ID NO:11. Applicants direct the Examiner’s attention to Attachment A, which is a modified version of Fig. 3 of the van de Locht reference, wherein Applicants have highlighted the essential passages in the description of the figure. This is the essential technical teaching of van de Locht et al. Applicants have also boxed and referenced the location of SEQ ID NO:11 in relation to the essential sequence taught by van de Locht et al.

Van de Locht et al. identify a DNA sequence within the PR2 promoter from positions -168 to position -52 as being necessary for strong elicitor-inducibility of the promoter (see van de Locht et al. at Abstract and page 2947, left hand column, last paragraph). Furthermore, from the deletion analysis of the promoter (see id., e.g., Figures 5 and 6), van de Locht et al. teach that the

sequence between positions -168 and -108 is critical for both elicitor-inducibility and the strength of the promoter. On the other hand, the sequence from position -108 to position -52 was considered to mediate elicitor-dependent expression only at a low level (see *id.* at page 2149, left-hand column, last sentence of the third paragraph and first two sentences of the fourth paragraph).

In the present application, the D-Box sequence (SEQ ID NO:11) is contained in the promoter sequence shown in Figure 3 of van de Locht et al. from position -76 to position -46 (*see* Attachment A). This means that the D-Box sequence of the present invention is not within the sequence between positions -168 and -108, which is described by van de Locht et al. as being the most important. Further, the D-Box sequence of the present invention is not even within the sequence range of positions -168 and -52. Thus, van de Locht et al. teaches away from the D-Box sequence (SEQ ID NO:11) of the present invention.

The D-Box sequence of the present invention (from position -76 to position -46) has been shown later by Rushton et al. (Rushton et al., *The Plant Cell*, 14:749-762 (2002)) that in the form of a tetramer, it mediates a strong pathogen-inducible transcription, whereas the sequence between -76 and -52, albeit being pathogen inducible, only forms a weak promoter. Rushton et al. show that the sequence between position -76 and -52 is 30 times weaker a promoter as compared with the sequence between position -76 and -46 (see Rushton et al., at the section bridging pages 755 and 756, as well as Figure 9, showing that the promoter "4xD" with the additional 6 bases, is 30 times stronger than the promoter "4xD short").

Van de Locht et al. do not teach the *cis*-element D-Box having the sequence shown in SEQ ID NO:11, as presented in the instant invention. The importance of SEQ ID NO:11 as an elicitor-responsive element can also not be deduced from the experimental data provided in van de Locht et al. For example, the constructs pPR2-11 and pPR2-12 in Figure 5 only exhibit a very weak inducibility (and this with a rather significant standard deviation). This is despite of the fact that these constructs do contain an entire copy of SEQ ID NO:11. Precisely because of this drop of inducibility, the authors concluded that the 116 base pairs (boxed in Fig 3) are decisive. A PHOSITA would not have been prompted to search for further sequence portions downstream of that 116 bp region identified and would, due to the deletion constructs of pPR2-11 and pPR2-

12, rather believe that sequences between -168 and -108 and/or -108 and -83 contribute to the function of the identified *cis*-element. This is stressed by page 2949 left column of van de Locht et al., stating:

A regulatory sequence between -168 and -52 appears to be both necessary and sufficient to mediate this response. . . . Sequences between -168 and -108 appear to be critical for both elicitor-mediated and quantitative base-level GUS expression (compare pPR2-10 and pPR2-11). Whether sequences downstream of -108 still constitute a weak minimal elicitor-responsive promoter remains unclear.

Again, the sequence between positions -168 and -52 does not contain SEQ ID NO:11.

Hence, a PHOSITA would not have been motivated to use SEQ ID NO:11 as a *cis*-acting element for duplication or in combination with other elements.

As noted by the Examiner, van de Locht et al. also do not teach a chimeric promoter construct that contains two of the D-Box elements. Thus the necessity for the §103 rejection over van de Locht et al. in view of Pears and Williams and Searle et al., and further in view of Comai et al.

The Examiner asserts that Pears and Williams teach that promoter sequences inserted into promoters can mediate sufficient gene expression, and that the promoter elements function optimally when multiple copies of the sequences are present.

In response, Applicants point out that Pears and Williams discuss that "these sequences [CP1 and CP2] are either essential promoter elements, not themselves interaction with the inducer, or that their interaction with a separate class of control sequences is necessary for inducible expression" (see Abstract). These cysteine proteinase elements do not function as elicitor-specific responsive elements, may not be used to confer cAMP inducibility on a heterologous gene, and thus cannot be compared to the instant invention (see Abstract). These cysteine proteinase elements are also different sequences in relation to each other, *i.e.* CP1 and CP2, and encode co-ordinately expressed mRNA sequences. Applicants teach use of the same sequence as an elicitor responsive element. Further, for the reasons discussed above, van de Locht et al. do not teach or disclose the instant invention and as such the combination of these references fail to rise to the level of obviousness.

Regarding Pears and Williams, Applicants additionally request the Examiner to review the 37 C.F.R. § 1.132 Declaration of the inventor Imre Somssich, filed on March 12, 2007. In the declaration, Dr. Somssich explains (in point 7):

Although Pears and Williams teach that multimers of a promoter element (actually only one copy versus two were tested!) can enhance expression, the patent examiner is incorrect in his claim that: "Pears and Williams teach that heterologous promoter sequences inserted into promoters can mediate sufficient gene expression" (see Claims Rejections page 5 and 6). In fact, as demonstrated by Pears & Williams in their cited publication, the tested promoter element (designated oligo L from the CP1 gene promoter) was incapable of mediating expression when placed in front of a heterologous gene (namely the actin1S gene). Oligo L could only restore induced expression on the CP2 gene. CP2 is the sister gene of CP1 and both have originally evolved from a common ancestral gene via gene duplication. CP2 expression behavior is identical to CP1, and it contains the same oligo L-like elements in its promoter. Thus, the promoter sequence used cannot be regarded as heterologous to this respect. However, even in this case, oligo L derived from CP1 could only functionally replace the oligo L-like elements from CP2 when placed precisely at a similar position within the CP2 promoter. Pears & Williams teach that their oligo L promoter element (also as a multimer) is inactive when placed at a different position even within the CP2 promoter.

Our invention is novel over Pears & Williams (1998) since our described synthetic element clearly functions as a pathogen-responsive element when placed upstream of a heterologous gene. Furthermore, the exact positioning of our element, and multimers hereof, within a TATA-box containing promoter is not critical for allowing pathogen-induced expression. Thus, from the information learned from Pears & Williams, it would not have been obvious that our synthetic element behaved as it did.

The Examiner also asserts that the Searle and Comai references teach enhanced expression with duplicated promoters.

In response, Applicants submit that Searle et al. and Comai et al. fail to make up for the deficiencies of van de Locht et al. Neither of these references teaches a chimeric promoter consisting of SEQ ID NO:11. Furthermore, Searle et al. discusses that a single element did not respond to zinc as opposed to "increasing the inducibility." Neither Searle et al. nor Comai et al. teach or disclose use of the same sequence as an elicitor responsive element, that is SEQ ID NO:11.

Regarding Searle et al., Applicants additionally request the Examiner to review the 37 C.F.R. § 1.132 Declaration of the inventor Imre Somssich, filed on March 12, 2007. In the declaration, Dr. Somssich explains (in point 8):

Serle et al. (1985) showed that two highly sequence-related elements (termed MREs for metal regulatory elements) conferred zinc-dependent expression when placed upstream of an otherwise non-responsive gene (TK gene). One copy of such MRE was inefficient whereas multimers increased zinc-dependent expression.

Although Serle et al. could demonstrate in the case of the MREs that multimers are more effective than monomers, one cannot generalize this nor can one derive from their studies that this will be the case. In fact, Lozoya et al. (The Plant Journal 1, 227-234, 1991) teach in figure 6 and table 1 that whereas the light responsive CHS promoter elements (termed 1 and 2) in the context of their own promoter enable light-specific expression of the GUS reporter gene, a dimer of element 1 placed in both orientations in front of TATA box region cannot mediate light responsiveness. Similarly, Longmann et al. (Proc. Natl. Acad. Sci. USA 2, 5905-5909, 1995) teach that tetramers of three different response elements of the PAL promoter do not enhance light- or elicitor-specific expression.

Regarding Comai et al., Dr. Somssich explains (in point 9):

Comai et al. teaches that by joining portions to two different promoters (from the 35S promoter and mas promoter) synergy and distinct properties may be obtained. Duplication of the 35S enhancer region (-430 to -90) resulted in 2-fold enhancement of expression levels.

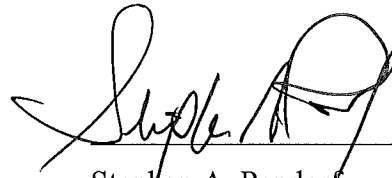
I have difficulty in seeing how their results impinge on our claims. Although duplication of promoter regions can enhance expression, Comai et al. teach that the range of expression levels of such chimeric promoters was very broad and thus unpredictable. Furthermore Comai et al. clearly also state (page 379) that: "reiteration of the 35S upstream region (the "35S enhancer") did not have a major effect on expression" Furthermore, as also referred to in their paper, the group of Odell et al. (Plant Molecular Biology 10:263-272, 1988) found that duplication of the 35S promoter (region -392 to -55) did not enhance expression. Moreover, Comai et al. do not teach that increased pathogen responsiveness can be achieved by duplication of promoter elements.

Thus, Applicants respectfully assert that, taken alone or in combination, none of these references teach or disclose the instant invention.

The Commissioner is hereby authorized to charge any fees which may be required at any time during the prosecution of this application without specific authorization, or credit any overpayment, to Deposit Account Number 16-0877.

Should further issues remain prior to allowance, the Examiner is respectfully requested to contact the undersigned at the indicated telephone number.

Respectfully submitted,



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Date: **September 28, 2010**

ATTACHMENT A

Modified Fig. 3 from van de Locht et al., showing that SEQ ID NO:11 does not fall within the essential sequence identified by van de Locht et al.

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Fig. 3. Partial nucleotide and deduced amino acid sequences of PR2. The nucleotide sequence (excluding the intron) from positions +51 to +987 (open arrowheads) was identical to that of the near full-length cDNA. The transcription start site (+1) is indicated by an arrow. The putative TATA box (closed line), CCAAT box (underlined by dots) and polyadenylation signal sequence (dashed line) are indicated. Sequences, within the PR2 promoter, identified to be necessary for elicitor-mediated gene expression (see text), are boxed and the positions of the relevant 5' endpoint deletion constructs indicated by closed arrowheads.